Summary of Product Characteristics
PREGABIN 100
(Pregabalin 100 mg hard capsules)

1. Name of the medicinal product

PREGABIN 100 (Pregabalin Capsules 100 mg)

2. Qualitative and quantitative composition

Each hard capsule contains 100 mg of pregabalin.

For the full list of excipients, see section 6.1.

3. Pharmaceutical form

Hard capsule.

Blue/white, size ‘2’ hard gelatin capsule containing white powder.

4. Clinical particulars

4.1 Therapeutic indications

Pregabalin is indicated for the treatment of peripheral and central neuropathic pain in adults. It is also indicated as adjunctive therapy in adults with partial seizures with or without secondary generalisation, and for the treatment of generalised anxiety disorder in adults.

4.2 Posology and method of administration

Posology

The dose range is 150 to 600 mg per day, given in two or three divided doses. Treatment may be started at 150 mg per day; based on individual response and tolerability, the dose may be increased to 300 mg per day after an interval of 3 to 7 days, and if necessary to a maximum of 600 mg per day after an additional 7-day interval.

Discontinuation

If pregabalin has to be discontinued, it is recommended this be done gradually over a minimum of one week, independent of the indication.

Renal impairment

Pregabalin is eliminated primarily by renal excretion as unchanged drug; the dose must be adjusted in patients with reduced renal function according to creatinine clearance. Pregabalin is removed effectively by haemodialysis, and a supplementary dose is required after each 4-hour session.

Elderly

Elderly patients may require a dose reduction owing to a decrease in renal function.

Paediatric population

The safety and efficacy of pregabalin in children below the age of 12 years and in adolescents have not been established.

Method of administration

For oral use, with or without food.

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

4.4 Special warnings and precautions for use

Hypersensitivity

Cases of hypersensitivity reactions, including angioedema, have been reported. Pregabalin should be discontinued immediately if symptoms of angioedema, such as facial, perioral or upper-airway swelling, occur.

Dizziness, somnolence and effects on the CNS

Pregabalin treatment has been associated with dizziness and somnolence, which could increase the occurrence of accidental injury (falls) in the elderly. Cases of loss of consciousness, confusion and mental impairment have also been reported.

Suicidal ideation and behaviour

Suicidal ideation and behaviour have been reported in patients treated with antiepileptic agents in several indications. Patients should be monitored for signs of suicidal ideation and behaviour, and appropriate treatment considered; patients and carers should be advised to seek medical advice should such signs emerge.

Drug abuse, dependence and withdrawal

Cases of abuse and dependence have been reported. Caution is required in patients with a history of substance abuse, and such patients should be monitored for symptoms of pregabalin misuse. Withdrawal symptoms (including insomnia, headache, nausea, anxiety, diarrhoea, sweating and, rarely, convulsions) have been reported after discontinuation; the dose should be tapered gradually.

Respiratory depression

Cases of severe respiratory depression have been reported. Patients with compromised respiratory function, respiratory or neurological disease, renal impairment, concomitant use of central nervous system depressants and the elderly may be at higher risk; a dose adjustment may be necessary in these patients.

Other

Congestive heart failure has been reported in some patients, particularly the elderly with cardiovascular conditions. Cases of renal failure, and of reduced lower-gastrointestinal-tract function (e.g. intestinal obstruction, paralytic ileus, constipation) when co-administered with constipating medicines such as opioids, have been reported. Peripheral oedema and weight gain may occur.

4.5 Interaction with other medicinal products and other forms of interaction

As pregabalin is predominantly excreted unchanged in the urine, undergoes negligible metabolism, does not bind to plasma proteins and does not inhibit drug metabolism in vitro, it is unlikely to produce, or be subject to, pharmacokinetic interactions. Pregabalin may potentiate the effects of ethanol and lorazepam and, in the post-marketing experience, cases of respiratory failure, coma and death have been reported in patients taking pregabalin with opioids and/or other central-nervous-system depressants. Pregabalin may add to the impairment of cognitive and gross-motor function caused by oxycodone. Co-administration with medicines that cause constipation (e.g. opioid analgesics) may lead to reduced lower-gastrointestinal-tract function.

4.6 Fertility, pregnancy and lactation

Pregnancy

Data from observational studies suggest an increased risk of major congenital malformations following exposure to pregabalin during the first trimester. Pregabalin should not be used during

pregnancy unless clearly necessary (if the benefit to the mother clearly outweighs the potential risk to the foetus). Women of childbearing potential must use effective contraception during treatment.

Breast-feeding

Pregabalin is excreted in human milk. A decision must be made whether to discontinue breast-feeding or to discontinue/abstain from pregabalin therapy, taking into account the benefit of breast-feeding for the child and the benefit of therapy for the woman.

Fertility

There are no clinical data on the effects of pregabalin on female fertility. In a clinical trial in men, pregabalin had no effect on sperm motility.

4.7 Effects on ability to drive and use machines

Pregabalin may have a minor to moderate influence on the ability to drive and use machines. It may cause dizziness and somnolence, and patients are advised not to drive, operate complex machinery or engage in other potentially hazardous activities until it is known whether the medicine affects their ability to perform these activities.

4.8 Undesirable effects

The adverse reactions are listed below by System Organ Class and frequency, defined as: very common (≥1/10), common (≥1/100 to <1/10), uncommon (≥1/1,000 to <1/100) and not known (cannot be estimated from the available data).

System Organ Class	Frequency	Adverse reaction
Infections and infestations	Common	Nasopharyngitis
Blood and lymphatic system disorders	Not known	Neutropenia
Immune system disorders	Uncommon	Hypersensitivity
	Not known	Angioedema, allergic reaction
Metabolism and nutrition disorders	Common	Increased appetite
	Uncommon	Anorexia, hypoglycaemia
Psychiatric disorders	Common	Euphoric mood, confusion, irritability, disorientation, insomnia, libido decreased
	Uncommon	Depression, agitation, mood swings, depersonalisation, hallucination, abnormal dreams
	Not known	Suicidal ideation or behaviour, aggression
Nervous system disorders	Very common	Dizziness, somnolence, headache
	Common	Ataxia, coordination abnormal, tremor, dysarthria, amnesia, memory impairment, disturbance in attention, paraesthesia, sedation, balance disorder, lethargy
	Uncommon	Syncope, stupor, myoclonus, cognitive disorder
Eye disorders	Common	Vision blurred, diplopia
	Uncommon	Visual field defect, dry eye, eye swelling
Ear and labyrinth disorders	Common	Vertigo
Cardiac disorders	Uncommon	Tachycardia, atrioventricular block first degree
	Not known	Congestive heart failure, QT prolongation
Vascular disorders	Uncommon	Hypotension, hypertension, flushing
Respiratory, thoracic and mediastinal disorders	Uncommon	Dyspnoea, epistaxis, cough, nasal congestion
	Not known	Pulmonary oedema
Gastrointestinal disorders	Common	Vomiting, nausea, constipation, diarrhoea, flatulence, abdominal distension, dry mouth
	Not known	Tongue swelling
Skin and subcutaneous tissue disorders	Uncommon	Rash, pruritus, sweating
	Not known	Stevens-Johnson syndrome, angioedema

System Organ Class	Frequency	Adverse reaction
Musculoskeletal and connective tissue disorders	Common	Muscle cramp, arthralgia, back pain, pain in extremity
	Uncommon	Muscle twitching, joint swelling, myalgia
	Not known	Rhabdomyolysis
Renal and urinary disorders	Uncommon	Urinary incontinence, dysuria
	Not known	Urinary retention
Reproductive system and breast disorders	Common	Erectile dysfunction
	Uncommon	Sexual dysfunction, delayed ejaculation
General disorders and administration site conditions	Common	Oedema, peripheral oedema, abnormal gait, feeling drunk, feeling abnormal, fatigue
	Not known	Face oedema
Investigations	Common	Weight increased
	Uncommon	Blood creatine phosphokinase increased, alanine aminotransferase increased, aspartate aminotransferase increased, platelet count decreased

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions to the National Regulatory Authority.

4.9 Overdose

In overdose, the most commonly reported adverse reactions included somnolence, confusional state, agitation and restlessness; seizures and, rarely, coma have also been reported. Treatment of overdose includes general supportive measures and may include haemodialysis if necessary.

5. Pharmacological properties

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Antiepileptics, other antiepileptics. ATC code: N03AX16.

Pregabalin is an analogue of gamma-aminobutyric acid (GABA). It binds with high affinity to the alpha-2-delta auxiliary subunit of voltage-gated calcium channels in the central nervous system, reducing calcium influx at nerve terminals and modulating the release of several excitatory neurotransmitters. This activity is thought to underlie its analgesic, anticonvulsant and anxiolytic effects.

5.2 Pharmacokinetic properties

Pregabalin is rapidly absorbed when administered in the fasted state, with peak plasma concentrations reached within 1 hour; its oral bioavailability is estimated to be ≥90% and is independent of dose. It does not bind to plasma proteins, undergoes negligible metabolism (approximately 98% of an absorbed dose is excreted unchanged in the urine), and has a mean elimination half-life of about 6.3 hours. Pregabalin clearance is proportional to creatinine clearance and is reduced in patients with renal impairment.

5.3 Preclinical safety data

Non-clinical data reveal no special hazard for humans based on conventional studies of safety pharmacology, single- and repeated-dose toxicity, and genotoxicity. Carcinogenicity findings in mice are considered of doubtful relevance to humans. Effects on reproduction and development were observed only at exposures sufficiently in excess of the maximum human exposure.

6. Pharmaceutical particulars

6.1 List of excipients

The full quantitative list of excipients was not provided in the source registration record and should be inserted verbatim from the applicant's finished-product formulation (3.2.P.1) before finalisation. Any excipient of known effect present in the formulation must additionally be declared in section 2 and, where relevant, warned in section 4.4.

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

To be confirmed from the applicant's stability data.

6.4 Special precautions for storage

Store below 30°C. Protect from light and moisture. Keep out of the reach and sight of children.

6.5 Nature and contents of container

3 x 10 capsules in Alu-Alu blister packs, presented in a printed carton together with the package insert.

6.6 Special precautions for disposal and other handling

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7. Marketing Authorisation Holder and Manufacturer

Marketing Authorisation Holder

Krishna Chemists Ltd, Nairobi, Kenya.

Manufacturer

Globela Pharma Private Limited, Plot No. 357 & 358, G.I.D.C., Sachin, Surat-394230, Gujarat State, India.

8. Marketing Authorisation Number

H2021/CTD6299/2056ER

9. Date of first authorisation / renewal of the authorisation

10. Date of revision of the text